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(56) **Aqueous dispersions of polymers cross-linked with metallic ions.**

(57) A composition which is a cross-linked aqueous dispersion characterised in that it comprises:
a water-dissipatable polymer in an amount of from 18 to 30%, by weight, based on the total weight of the composition;
water in an amount of from 67 to 30%, by weight, based on the total weight of the composition;
a source of multivalent metallic ions in an amount of from 0.1 to 5%, by weight, based on the total weight of the composition; and
a humectant in an amount of from 0.1 to 40%, by weight, based on the total weight of the composition is disclosed.

Such may be in the form of an emulsion which may additionally comprise:
one or more emollient oils in an amount of from 0.1 to 25%, by weight, based on the total weight of the composition; and

an emulsifier in an amount of from 0.01 to 5%, by weight, based on the total weight of the composition.

Such compositions may be used in the production of cross-linked casts.

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AQUEOUS DISPERSIONS OF POLYESTER AND POLYESTERAMIDES CROSS-LINKED WITH METALLIC IONS AND CASTS MADE THEREFROM

This invention relates generally to cross-linking an aqueous dispersion of polyester or polyesteramide with the water soluble multivalent metallic ions. The aqueous dispersion of polyester or polyesteramides containing ether and sulfonate groups can also contain humectants and/or emollients which when cross-linked with metallic ions and poured into any desirable shaped mold form a clear or opaque cast of therapeutic functional nature. This invention also relates to the process of cross-linking the polyester or polyesteramide aqueous dispersion with metallic ions.

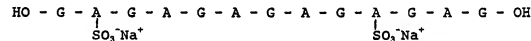
Many compositions used for skin treatment contain emollients or humectants in lotion, cream or gel form. Such products are applied by evenly spreading the product on the skin. Upon loss of water, the product dries providing humectants and emollients to the epidermis.

Water soluble gels that form protective films of various types are known. For example, U.S. Patent No. 4,393,048 discloses a water soluble hydrogel of alkali metal alginate and glycerine that dries to a non-toxic, pliable protective film. U.S. Patent No. 3,949,742 discloses a transparent medical dressing which performs as a synthetic film over skin wounds. Water soluble polyesters, for example U.S. Patent 4,502,976, are used to form cross-linked bioerodible hydrogels. The hydrogels, suitable for carrying water soluble therapeutic macromolecules and for implantation in living mammals, are produced by a complex polymerization process without using water soluble metallic ions.

US Patent No 3,879,168 to Franklin discloses a surgical dressing made of partially soluble alginic materials in the form of gauze or wool characterized by a pH of 4 to 7 and a calcium content of 2-6% by weight comprised of a laminate of a thin layer of non-porous segmented polyurethane sewn to foam.

U.S. Patent Nos. 3,734,874, 4,233,196, 4,335,220, 4,304,900, 4,304,901, and 4,300,580 describe water-dissipatable, melttable polyesters that are useful as adhesives, coating materials, films, packaging materials and other products that can be dissolved, dispersed or otherwise dissipated in water or aqueous solutions. These polyesters, however, are not cross-linked using metallic ions and cast into shapes to entrap water, humectants and/or emollients within the hardened cast.

As explained in a technical publication from Eastman, the water dispersability of the AQ polymer is largely attributed to the presence of ionic substituents attached to the polymer chain. A simplified representation of the polymer is shown below:



wherein "A" is an aromatic dicarboxylic acid moiety some of which have sulfonate (-SO₃⁻ . Na⁺) substituents, "G" is an aliphatic or cycloaliphatic glycol residue and "OH" is a hydroxy end group.

It is the sodio sulfo group which impart the water dispersability to the polymer. To cross-link with multivalent metallic ions and obtain the moldable shapes of this invention, the multivalent metal salts must be added and mixed according to the teaching of this invention. Departing from this process results in non-compatible mixtures of non-commercial properties. Eastman technical publications teach the synthesis and preferred methods for cross-linking water dispersible polyesters and polyesteramides with other resins through high temperature curing process and subsequent drying of the cured resins, but specifically warn against the use of the heavy metal salts included in this invention as being not compatible with the polymers used in this invention.

It is therefore an object of the present invention to provide novel cross-linked polyester polymers with humectants and/or emollients by using water soluble metallic ions.

A further object of the present invention is to provide a convenient process of cross-linking the humectant and emollients with the polyester polymer in the presence of water soluble metallic ions.

A further object of this invention is to provide such casted patches containing water soluble medicaments and oil soluble medicaments. Such patches can be used as controlled release transdermal delivery patches.

It has been found that the objectives of this invention may be realized by forming a cast containing humectants and/or emollient oils, water, water dissipatable polyesters, and by cross linking with water soluble multivalent metal ions. Such compositions when poured into a mold harden without pressure and have utility in wound treatment, skin treatment and controlled release drug and fragrance patches.

The casts of this invention comprise water dissipatable polyester or polyesteramide in an amount from

18 to 30%, by weight, water in an amount from 67 to 80% humectants in an amount from 0.01 to 40%, by weight, and a source of multivalent metal ions for cross-linking purposes in an amount from 0.01 to 5%. Casts of this invention can also be formulated using emollient oils in an amount from 0.01 to 25%, by weight, based on the total weight of the composition, water dissapatable polyester in an amount from 18-30%, by weight, water in an amount from 67-80%, by weight, based on the total weight of the composition, and a source of multivalent metallic ions in an amount from 0.01 to 5% based on the total weight of the composition. Optionally the composition also contains fragrance oils, medical agents or color.

Cross-linked clear casts of the present invention comprise (a) a water dissapatable polyester polymer in an amount from 18 to 30%, by weight, based on the total weight of the composition; (b) water in an amount from 67-80%, by weight, based on the total weight of the composition; (c) a source of multivalent metallic ions in an amount of 0.1-5%, by weight, based on the total weight of the composition; (d) humectant such as propylene glycol, glycerine in an amount from 0.1-40%, by weight, based on the total weight of the composition.

The cross-linked cast of the present invention can also be in the form of an opaque emulsion system. Such emulsion cast of the present invention comprise (a) a water dissapatable polymer in an amount from 18 to 30%, by weight, based on the total weight of the composition; (b) water in an amount from 67 to 80%, by weight, based on the total weight of the composition; (c) emollient oils in an amount from 0.1 to 25%, by weight, based on the total weight of the composition; (d) a source of multivalent metallic ions in an amount from 0.1 to 5%, by weight, based on the total weight of the composition; (e) humectants in an amount from 0.01 to 40%, by weight, based on the total weight of the composition; (f) any suitable oil-in-water emulsifier in an amount from 0.01 to 5%, by weight, based on the total weight of the composition.

Polymers useful in the present invention must be capable of cross-linking with water soluble metal ions, and, when poured in liquid form into a mold hardening without pressure to form a cast of any desirable shape. Polymers suitable for use in this invention include the water-dissipatable polyester and polyestaramides described in U.S. Patent No. 3,734,874 to Kibler, et al., U.S. Patent No. 4,233,196 to Sublet and U.S. Patent No. 4,304,801 to O'Neill, et al. A preferred water dissapatable polyester is commercially available on Eastman AQ 55S polymers.

Examples of organic and inorganic sources of the multivalent metal ions used to cross-link the polymers in this invention include magnesium chloride, zinc acetate, zinc gluconate, zinc oxide, titanium dioxide and magnesium acetate. The preferred sources of multivalent metal ions are water soluble and include zinc gluconate and magnesium chloride.

In forming the clear cross-linked casts of this invention, water by itself or in combination with humectant such as propylene glycol and glycerine may be used.

In forming cross-linked emulsion casts of this invention any emollient oil may be used. Emollients useful in this invention include hydrocarbon oils and semi-solid hydrocarbons, lanolin and derivatives, silicone oils and esters commonly used in the cosmetic and dermatological fields.

The cross-linking of polymer containing emulsion systems by means of multivalent metallic ions can be achieved with or without the additional emulsifiers. The selection of an appropriate emulsifier for a given system is within the purview of one skilled in the art.

Optionally, a wide variety of agents may be incorporated into the compositions of this invention for a variety of purposes. For example, medicaments such as benzoyl peroxide, methyl nicotinate, salicylic acid, benzocaine and menthol can be cast into desirable shapes for therapeutic use.

The cross-linked hydrogels and emulsions can be cast into any desirable shape and used for various purposes. For example, casts in the form of face masks may be used for treating dry skin. Casts in the form of patches or pads may be used to cover burns and wounds for soothing and comforting the inflamed area, or for delivering active medicaments to the damaged skin as a controlled release, transdermal patch.

Both the clear and opaque emollient casts may also contain fragrance, insect repellents, sun screens and like chemicals.

The following examples illustrate how the cross-linked casts of this invention may be formed.

EXAMPLE 1

A clear cross-linked cast was produced having the following composition:

Eastman AQ 55S Polymer	24.0
Zinc Gluconate (USP)	2.0
Propylene Glycol	34.0
Water	42.0

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The cross-linked cast of Example 1 was prepared by placing the appropriate amounts of water and propylene glycol into a suitable container and heating the mixture to 80° C. The appropriate amount of polymer was gradually added with a high shear mixing to dissolve the solids. When all the solids were added, high shear mixing is continued, until a clear, straw colored, thick gel was produced. The gel was then cooled to room temperature and an appropriate amount of zinc gluconate aqueous solution added by high shear mixing until cross-linking occurred. The liquid was poured into a mold of desirable shape to produce a cast of hydrogel. The metallic cross-linking can be done either at room temperature or at elevated temperatures depending on the composition.

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15EXAMPLE 2

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An emulsion crosslinked cast was produced having the following composition:

Eastman AQ 55S Polymer	20.3
Propylene Glycol	28.0
Mineral oil	10.0
PJ	7.0
Polysorbate 20	1.0
Zinc gluconate	2.0
Water	31.7

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The cross-linked emulsion casts of Example 2 were formed by placing appropriate amounts of water and propylene glycol in a suitable container and heating the mixture to 80° C. The appropriate amount of polymer was gradually added with a high shear mixing until a clear viscous liquid was produced. The polysorbate 20 was added to the clear liquid and mixing continued. The melted oil phase was then added to the aqueous phase and homogenized to form a smooth emulsion. To this emulsion the appropriate amount of aqueous solution of zinc gluconate was added with continued mixing. Pouring into a mold at appropriate viscosity formed a cast of the desired shape. The cross-linking of the emulsion can be carried out between 50° C to 70° C, as desired, for manufacturing and suitable for pouring into the molds for casting purposes.

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40EXAMPLE 3

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Water insoluble sources of multivalent metallic ions such as, for example, zinc oxide or titanium dioxide can be added to form more rigid cross-linked casts.

Eastman AQ 55S Polymer	21.00
Propylene Glycol	28.00
Petroleum Jelly	15.00
Glycerol Monostearate and Polyoxyethylene stearate	1.00
Zinc Oxide	2.00
Zinc Gluconate	2.00
Microcrystalline Wax	5.00
Water	28.00

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EXAMPLES 4-24

The following are additional specific examples of formulations used to produce cross-linked casts of this invention:

Ex. 4	
Eastman AQ 55S polymer	21
Propylene glycol	28
Zinc gluconate	2
Water	49

Ex. 5	
Eastman AQ 55S polymer	25.5
Propylene glycol	34.0
Zinc gluconate	2.0
Water	38.5

Ex. 6	
Eastman AQ 55S polymer	20.3
Propylene glycol	18.0
Zinc gluconate	2.0
Water	59.7

Ex. 7	
Eastman AQ 55S polymer	23.3
Propylene glycol	10.0
Zinc gluconate	2.0
Water	64.8

Ex. 8	
Eastman AQ 55S polymer	21
Propylene glycol	28
Zinc gluconate	2
Water	49

Ex. 9	
Eastman AQ 55S polymer	24
Propylene glycol	32
Zinc gluconate	2
Water	42

Ex. 10	
Eastman AQ 55S polymer	27
Propylene glycol	36
Zinc gluconate	2
Water	35

Ex. 11	
Eastman AQ 55S polymer	23.2
Zinc gluconate	2.0
Water	74.8

Ex. 12	
Eastman AQ 55S polymer	23.2
Magnesium chloride	0.5
Water	76.3

Ex. 13	
Eastman AQ 55S polymer	24
Glycerine	32
Zinc gluconate	2
Water	42

Ex. 14	
Eastman AQ 55S polymer	24.0
Propylene glycol	32.0
Magnesium chloride	0.3
Water	43.7

Ex. 15

Eastman AQ 29S polymer	15.0
Eastman AQ 55S polymer	5.4
Propylene glycol	27.2
Mineral oil	10.0
Polysorbate 20	2.0
Zinc gluconate	3.0
Water	37.4

Ex. 16

Eastman AQ 55S polymer	20.3
Propylene glycol	28.0
Mineral oil	10.0
Petroleum jelly	7.0
Polysorbate 20	1.0
Zinc gluconate	2.0
Water	31.7

Ex. 17

Eastman AQ 55S polymer	20.3
Propylene glycol	28.0
Mineral oil	10.0
Petroleum jelly	7.0
Polysorbate 20	1.0
Zinc gluconate	1.5
Water	32.2

Ex. 18

Eastman AQ 55S polymer	18.0
Propylene glycol	24.0
Petroleum jelly	17.0
Polysorbate 20	1.0
Zinc gluconate	2.0
Water	38.0

Ex. 19

Eastman AQ 55S polymer	21
Propylene glycol	28
Dimethicone	19
Petroleum jelly	9
Glycerolmonostearate and Polyoxyethylene Stearate	1
Zinc gluconate	2
Water	30

Ex. 20

Eastman AQ 55S polymer	21.0
Propylene glycol	28.0
Petroleum jelly	17.0
Zinc gluconate	2.0
Water	32.0

Ex. 21

Eastman AQ 55S polymer	21.0
Propylene glycol	28.0
Petroleum jelly	16.0
Salicylic acid	2.0
Zinc gluconate	2.0
Water	10.0

Ex. 22

Eastman AQ 55S polymer	20.7
Propylene glycol	27.6
Petroleum jelly	15.0
Benzoyl peroxide	2.0
Glycerine	2.0
Zinc gluconate	2.0
Water	30.7

Ex. 23

Eastman AQ 55S polymer	21.0
Propylene glycol	28.0
Menthol	2.0
Zinc gluconate	2.0
Water	26.0

Ex. 24	
Eastman AQ 55S polymer	21.0
Propylene glycol	28.0
Petroleum jelly	15.0
Polysorbate 20	1.0
Superabsorbant polymer	1.0
Zinc gluconate	1.0
Water	33.0

Claims

1. A composition which is a cross-linked aqueous dispersion characterised in that it comprises:
 - a water-dissipatable polymer in an amount of from 18 to 30%, by weight, based on the total weight of the composition;
 - water in an amount of from 67 to 30%, by weight, based on the total weight of the composition;
 - a source of multivalent metallic ions in an amount of from 0.1 to 5%, by weight, based on the total weight of the composition; and
 - a humectant in an amount of from 0.1 to 40%, by weight, based on the total weight of the composition.
2. A composition as claimed in claim 1 which is a cross-linked emulsion characterised in that it additionally comprises;
 - one or more emollient oils in an amount of from 0.1 to 25%, by weight, based on the total weight of the composition; and
 - an emulsifier in an amount of from 0.01 to 5%, by weight, based on the total weight of the composition.
3. A cross-linked composition as claimed in claim 1 or claim 2 wherein the source of multivalent metallic ions is selected from magnesium chloride, zinc acetate, zinc gluconate, zinc oxide, titanium dioxide and magnesium acetate.
4. A method of producing a cross-linked cast characterised in that it comprises;
 - (a) forming a composition as claimed in any of claims 1 to 3; and
 - (b) pouring the composition into a mold whereby there is obtained a cross-linked cast.

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Sevenoaks, Kent TN13 1XR(GB)(54) **Aqueous dispersions of polymers cross-linked with metallic ions.**

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a humectant in an amount of from 0.1 to 40%, by weight, based on the total weight of the composition is disclosed.

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one or more emollient oils in an amount of from 0.1 to 25%, by weight, based on the total weight of the composition; and
an emulsifier in an amount of from 0.01 to 5%, by weight, based on the total weight of the composition.

Such compositions may be used in the production of cross-linked casts.

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EUROPEAN SEARCH REPORT

Application Number

EP 90 30 6515

DOCUMENTS CONSIDERED TO BE RELEVANT					
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.8)		
X	FR-A-2 211 474 (ESSO RESEARCH AND ENGINEERING) * Claims 1,2,5,7; page 5, lines 31-38; page 6, lines 15-19,32-37; page 8, lines 25-31 * -----	1-4	C 08 J 3/24 C 08 K 3/00 C 08 K 5/09		
X	US-A-3 493 550 (J.M. SCHMITT et al.) * Claims 1,8,9; column 5, lines 30-45 * -----	1,3,4			
X	EP-A-0 022 624 (THE BRITISH PETROLEUM CO.) * Claim 1; examples 1-12 * -----	1,3			
X	FR-A-1 545 403 (POLYMER CORP.) * Claims A,C; page 2, column 1; page 4, table IV; example 5 * -----	1-3			
The present search report has been drawn up for all claims					
Place of search The Hague		Date of completion of search 19 September 91	Examiner PEETERS J.C.		
<table border="0"><tr><td>CATEGORY OF CITED DOCUMENTS X: particularly relevant if taken alone Y: particularly relevant if combined with another document of the same category A: technological background O: non-written disclosure P: intermediate document T: theory or principle underlying the invention</td><td>E: earlier patent document, but published on, or after the filing date D: document cited in the application L: document cited for other reasons A: member of the same patent family, corresponding document</td></tr></table>				CATEGORY OF CITED DOCUMENTS X: particularly relevant if taken alone Y: particularly relevant if combined with another document of the same category A: technological background O: non-written disclosure P: intermediate document T: theory or principle underlying the invention	E: earlier patent document, but published on, or after the filing date D: document cited in the application L: document cited for other reasons A: member of the same patent family, corresponding document
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